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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,528	09/19/2005	Shawn De Frees	040853-01-5126US	3615

43850 7590 03/31/2008

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EXAMINER	
HEARD, THOMAS SWEENEY	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
03/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,528	DE FREES, SHAWN	
	Examiner	Art Unit	
	THOMAS S. HEARD	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/20/2008 & 01/16/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1, Claims 1-17, in the reply filed on 2/01/2008 is acknowledged. Applicants elected G-CSF for the protein and water soluble polymer for the modified sugar. However, water soluble polymer is a genus. On March 18th, a telephone call was placed to Gargi Taluker, Ph.D., registry no. 61,368 to elect a species. Applicants have met the requirements of the election of species by electing polyethylene glycol for the water soluble polymer.

Claims 18 and 19 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Claim(s) 1-19 are pending. Claims 18 and 19 are withdrawn. Claims 1-17 are hereby examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

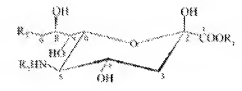
Claims 1, 4-8, 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using

Synthetic Sialic Acid Analogues, " The Journal of Biological Chemictry (2002), pages 668-6695, from Applicant's IDS.

The instant invention is drawn to a method of forming a peptide conjugate where a modified sugar is incubated under conditions where the cell internalizes the modified sugar, in incorporated into a nucleotide sugar, and is then covalently linked to the peptide through the catalysis of the glycosyltransferase present within the cell.

Oetke et al discloses a method of modifying a peptide/protein by incubating the cells expressing the peptide/protein with a modified sugar, which is internalized and covalently linked to the peptide through the catalysis of the glycosyltransferase present within the cell, readable upon Claims 1, 2, 4-8, 11-16. Oetke et al teaches a variety of modification (see Figure 1A and 1B below), where substitutions were made at R_1, R_2, and R_3:

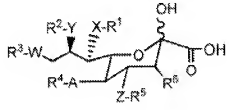
A



B

Sialic acids	Substituents			Effect on lectin binding			
	R_1	R_2	R_3	VVA	LFA	YLM
Neu5Ac	H	CH_3CO	HO-			
(a) 9-deoxy-Neu5Ac	H	CH_3CO	H	+	+	+
(b) 9-amino-Neu5Ac	H	CH_3CO	H_2N	+/-	+	+
(c) 9-acetamido-Neu5Ac	H	CH_3CO	CH_3CONH	+/-	+	+/-
(d) 9-N-Ethyl-Neu5Ac	H	CH_3CO	H_3CH_2CCONH	+/-	+	+
(e) 9-N-Biotinyl-Neu5Ac	H	CH_3CO	$BIOC(CH_2)_5CONH$	+/-	+	+
(f) 9-keto-Neu5Ac	H	CH_3CO	O	+	++	++
(g) 9-thio-Neu5Ac	H	CH_3CO	SH	+	++	++
(h) 9-NHCH_2-Neu5Ac	H	CH_3CO	CH_2NH_2	+	+	+
(i) 9-NO$_2$,CH_2-Neu5Ac	H	CH_3CO	CH_2NO_2	+	+	+/-
(j) 5-N-Benzoyl-Neu	H	C_6H_5CO	HO-	+	+	+
(k) 5-N-Trifluoroacetyl-Neu	H	CF_3CO	HO-	+	++	+/-
(l) 5-N-Glycolyl-Neu	H	H_2NCH_2CO	HO-	+/-	+	+
(m)5-N-Taco-Neu	H	$HOOC(CH_2)_2CO$	HO-	+/-	+	+
(n) 5,7-Bisac-Neu	H	CH_3CO	HO-	+	++	++
(o) Neu4Ac Me-ester	H_3C	CH_3CO	HO-	+	+	+
(p) Neu4Ac Et-ester	H_3C	CH_3CO	HO-	+	+	+

The compounds of A and B supra are readable upon the generic formula of the instant Claims 12-16. Claim 13 shows for example:



In the instant case, **for example**, R^3 is OH, R^2 is H, Y is a bond, X is –O-, R^1 is H, R^4 is substituted alkyl, A is –N(R^7), Z is –O-, R^5 is H, and R^6 is H, readable upon (a) 9-deoxy-NeuAc in Figure 1B supra, where R_1 is H, R_2 is CH_2CO, and R_3 is HO-. The generic of Claims 12, and 14-16 also make the compounds of Figure 1B for the identical reasons of the definitions of the various R groups between the instant claimed structure and the prior art of Oetke et al. Because the modified sugar must first be incorporated into a nucleotide for catalytic transfer to the peptide/protein, the steps of 4, 5, 6, and 7 are

inherent to the method because they are steps performed by the cell after incubating the initial substrate of the modified sugar with the cell, and do not require the steps to be performed by the skilled artisan. Therefore, the invention as claimed is anticipated by the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co. the court stated: "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In Gostelli, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) level of skill and knowledge in the art, (2) partial structure, (3) physical and/or chemical properties, (4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) method of making the claimed invention.

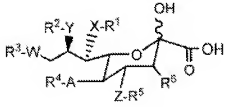
In the instant case, the claims are drawn to a method of forming a covalent conjugate between a modified sugar and a peptide protein *in vivo*.

(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to synthesis of compounds, experimental design, cell culture, protein urification techniques, and interpretation of the data results..

(2) Partial structure: (3) Physical and/or chemical properties: and (4) Functional characteristics:

The partial structures are sialic acid sugars that have been modified at various positions around the cyclohexyl ring as shown here:



The compounds are substrates for intracellular enzymes that will conjugate the modified sugar to form a nucleotide, and are then further conjugated by a transferase to form a glycosylated peptide/protein.

(5) Method of making the claimed invention:

Chemical synthesis of the analogs and enzymatic catalysis of the protein conjugates by *in vivo* transfer.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that Claims 1, and 11-16, are a broad generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of nucleotidyl moiety, activating leaving group, water-soluble

polymer, a therapeutic moiety, a detectable label, a biomolecule and a targeting moiety, of Claims 1, and 11-16.

It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. "MPEP § 2163.

Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. There are three example and those examples all show a single modification, that of polyethylene glycol. While having written description for polyethylene glycol identified in the specification examples on pages 104 and onward of the specification, the specification is void of any other molecules that qualify for the functional characteristics claimed. There a no examples of therapeutic moiety, nucleotidyl moieties, and targeting moieties, for example, that would allow one of ordinary skill in the art to practice the invention as claimed.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,265,085 B2 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,265,085 B2 teaches the enzymatic modification of peptide and protein through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble

polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,265,085 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,265,085 does not teach an in vivo method of practicing the same methods of synthesis.

Oetke et al teaches a method of modifying peptides or proteins by cellular (*in vivo)* incubation with the desired modified sugar, in the instant case, polyethylene glycol. The difference between what is taught in the prior art and what is claimed is that one is done with enzymes in vivo rather than in vitro.

It would have been obvious at the time of the instant invention to modify the method instantly claimed to incorporate the *in vivo* method taught by Oetke et al. One would have had been motivated to do so given the success in incorporating modified sialic residues into proteins as taught by Oetke et al. One would have had a reasonable expectation of success given Oetke et al teaching that the modified sugar residues would have been taken up by the cell and incorporated by cellular enzyme native to the cell, and perform the same method instantly claimed. Therefore, the invention as claimed is prima-facie obvious of the secondary reference of Oetke et al.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 112-214 of U.S. PG Pub 20080050772 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002),

pages 668-6695. 20080050772 teaches the enzymatic modification of granulocyte colony stimulating factor through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of 20080050772 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,265,085 does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,265,085 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated granulocyte colony stimulating factor as claimed in the instant Claim 17

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-155 of U.S. Patent No. US 7,297,511 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US US 7,297,511 teaches the enzymatic modification of interferon alpha through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for

longer half-life). The method of the invention of US US 7,297,511 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US US 7,297,511 does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,265,085 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated interferon alpha claimed in the instant Claim 17.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-113 of U.S. Patent No. US 7,226,903 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US US 7,226,903 teaches the enzymatic modification of interferon beta through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US US 7,226,903 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US US 7,226,903 does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,226,903 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated interferon beta claimed in the instant Claim 17.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-32 of U.S. Patent No. US 7,214,660 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,214,660 teaches the enzymatic modification of EPO through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,214,660 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,214,660 does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,214,660 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated EPO claimed in the instant Claim 17.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-107 of U.S. Patent No. US 7,179,617 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,179,617 teaches the enzymatic modification of Factor IX

through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,179,617 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,179,617 \ does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,179,617 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated Factor IX claimed in the instant Claim 17.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,173,003 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,173,003 teaches the enzymatic modification of GCS through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,173,003 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,173,003 does not teach an in vivo method of

practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,173,003 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated GCS claimed in the instant Claim 17.

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,157277 in view of Oetke et al, "Versitile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,157277 teaches the enzymatic modification of Factor VII through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,157277 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,157277 does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,157277 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated Factor VII claimed in the instant Claim 17.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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